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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,844	02/11/2004	Lon J. Wilson	1789-12301	3026

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,844	WILSON ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *11-22, and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *11 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-10 and 23 are drawn to a fullerene-antibiotic conjugate, classified in class 424, subclass 164.1.

   II. Claims 11-21 and 26 are drawn to a method of making a fullerene-antibiotic conjugate, classified in class 424, subclass 164.1.

   III. Claims 22,24 and 25 are drawn to method of inhibiting (killing) a bacterial species, classified in class 424, subclass 164.1.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the method for making the fullerene-antibiotic conjugate can be accomplished with materially different reactants. The use of an amino protected malonate derivative could be substituted with a protected malonate diester. The deprotection of the diester yields a malonic acid that may be functionalized or coupled with antibiotics via esterification or Mitsunobu type reactions, etc. The bases, solvents or coupling reagents of the instant claims may be substituted, for example weaker or stronger bases such as sodium hydride or DBU may be used.

3. Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the fullerene-antibiotic conjugate may be used for a materially different method of use. Anti-tumor antibiotics are well known for the treatment of cancer by interfering with DNA, blocking certain enzymes and cell division or changing cell membranes. Depending on the antibiotic, such as doxorubicin, the conjugate of the instant claims could potentially be used in for this mode of treatment (inhibiting the growth of tumor cells) and not for the inhibition of bacterial growth.

4. Inventions II and III are related as process of making and process of using the product. The use as claimed cannot be practiced with a materially different product. Since the product is not allowable, restriction is proper between said method of making and method of using. The product claim will be examined along with the elected invention (MPEP § 806.05(i)).

5. Because these inventions are independent or distinct for the reasons given above and the inventions require a different field of search and would impose an **undue burden of search** on the Office (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

6. Claims 1,4-7,9-26 are generic to the following disclosed patentably distinct species: antibiotics

7. The species are independent or distinct because the glycopeptide antibiotics drugs consist of glycosylated cyclic or polycyclic nonribosomal peptides whose mode of action is to inhibit the synthesis of petidoglycans thus inhibit the synthesis of cell walls. Penicillin is a β-lactam antibiotic that works by inhibiting the formation of peptidoglycan cross links in the bacterial cell wall thus, weakening the cell wall when it multiplies. Quinolones act by inhibiting the bacterial DNA gyrase causing inhibition of replication and transcription of the cells. The species are independent or distinct because the compounds are structurally distinct, contain different functional groups and chemical properties that would require an **undue search burden** to the office Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

8. During a telephone conversation with Marcella Watkins on 8/28/06 a provisional election was made **without traverse** to prosecute the invention of Group I, claims 1-10 and 23 and the species of glycopeptide. Affirmation of this election must be made by applicant in replying to this Office action. Claims 11-22 and 24-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

DETAILED ACTION

10. Applicant's election **without traverse** of Group I in the reply filed on 8/28/06 is acknowledged.

11. Claims 11-22 and 24-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups II and III, there being no allowable generic or linking claim. Election was made **without traverse** in the reply filed on 8/28/06.

Oath/Declaration

> It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Specification

12. The disclosure is objected to because of the following informalities: the recitation of "vanomycin" is incorrect (p2, [0006]). This is a misspelling. Appropriate correction is required.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/356856, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Provisional application 60/356856 describes the binding of a "drug" to a single-walled nanotubes for release of "drug" into tissues. Single-walled nanotubes are structurally different than fullerenes which are spherical in shape and are comprised of hexagon and pentagon rings that prevent them from being planar, thus imparting different physical and chemical properties on the fullerene. The encapsulation of a "lipophilic drug" or "drug", such as taxol within the center of a liposome is also described which does not provide information for antibiotics, binding of the "drug" or binding of any targeting agent to the fullerene and there is no mention of fullerene-antibiotic conjugates or the binding of the conjugate of the instant claims to anthrax spores or bone.

The priority date 2/11/03 of provisional Application No. 60/446406 is assigned to group I, claims 1-9 as it refers to the limitations of these claims.

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional

application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application No. 60/356856, 60/446406, 10367646, 10623110 and 10623190 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The prior-filed applications do not disclose the pharmaceutical composition of fullerene-antibiotic conjugates of the instant claims or their use in an aerosol mist for treatment.

The priority date 2/11/04 of the instant Application No. 10776844 is assigned to claims 10 and 23 as it refers to the limitations of these claims.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 1-3,6,8 and 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Cubbage et al. (Eighth Annual Orthopedic Resident Research Forum, vol 8, 2002).

15. Cubbage et al. (Eighth Annual Orthopedic Resident Research Forum, vol 8, 2002) teaches of the addition of the antibiotic vancomycin to a $C_{60}[C(PO_3H_2)_2]$ water-soluble, bone directed vector (p6, column 2).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-6,9,10 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cubbage et al. (Eighth Annual Orthopedic Resident Research Forum, vol 8, 2002) in view of Lei et al. (US 6,777,445B2).

18. Cubbage et al. (Eighth Annual Orthopedic Resident Research Forum, vol 8, 2002) teaches of the addition of the antibiotic vancomycin to a $C_{60}[C(PO_3H_2)_2]$ water-soluble, bone directed vector (p6, column 2). The antimicrobial activity of the compound was examined against methicillin-resistant *Staphylococcus aureus*. Cubbage et al. does not teach of the pharmaceutical formulations of the instant claims.

19. Lei et al. (US 6,777,445B2) discloses a water-soluble fullerene (C_{60}) derivative to treat bacterial infections, such as *E. coli, Staphylococcus aureus*, etc (column 2, lines 7-14; column 3, lines 8-20). Administration of a pharmaceutical formulation of the fullerene to a patient may include lubricating agents, carriers or may be made into

aerosols (column 6, particularly line 48). The fullerene described contains PO_3H, SO_3H, and CO_2H substituents that allows for bone-targeting (column 5, lines 7-8).

20. At the time of the invention it would have been obvious to one ordinarily skilled in the art to utilize the formulations of Lei et al. for the compound of Cubbage et al. since both are drawn to the treatment of bacterial infection *Staphylococcus aureus* with fullerene derivatives. The attachment of multiple vancomycin molecules would be obvious to increase efficacy of the formulation administered.

21. Claims 1-8 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al. (US 6,123,923) in view of Monforte et al. (US 6,635,452B1).

22. Unger et al. (US 6,123,923) discloses a vesicle composition comprising a stabilizing material, a photoactive agent, bioactive agents and/or targeting ligands and their use for therapeutic applications (column 1, lines 23-33; column 11, lines 47-50). The photoactive agent, fullerene, may be bound to targeting ligands/agents, such as antibodies (column 43, line 49; claim 14) specifically for targeting antigens or for targeting the agent to an area where an immune response is desired (column 47, lines 48-49; column 12, line 40; column 13, lines 60-62; column 14, line 21-22). Stabilizing material, such as phosphorylated or sulfonated lipids may be covalently bound to the photoactive agent to control vesicle size and physical interactions between it and the membranes of a cell or tissue (column 36, lines 40-54; claim 13). The bioactive agents may include antibiotics, such as penicillin. The bioactive agents are intended for therapeutic purposes via administration to a patient and subsequent application of

ultrasound (column 64, line 45; column 66, lines 40-46; column 68, lines 5-26). The covalent linking of the stabilizing material and targeting ligands to the photoactive agent are discussed throughout the disclosure (column 55). Unger et al. (US 6,123,923) does not explicitly disclose binding of the antibiotic to the photoactive agent.

23. Monforte et al. (US 6,635,452B1) disclose release tag compounds that contain a mass label, such as fullerene that is attached to the reactive groups, such as antibodies, for antigen-antibody interactions and/or bound to antibiotics (column 23, lines 13, 55 and 56; column 24, line 3).

24. At the time of the invention it would have been obvious to one ordinarily skilled in the art to attach (covalently) antibiotics and antibodies to the photoactive compound (fullerene) of Unger et al. as was done by Monforte et al. This would provide for improved delivery of the antibiotic to the targeted location (i.e. site specificity) in a patient, cells, tissues, etc. via the covalently bound targeting moiety-fullerene compound of Unger et al. The language of claim 8 "wherein the targeting agent is capable of binding to anthrax spores" is not a positive recitation and the agents of the disclosures are also capable of accomplishing the same for example, by attaching an antibiotic, such as ciprofloxacin to the conjugate.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
August 30, 2006

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER